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Paper No. 12

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES

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Ex parte JOHANNA OLWEUS, FRIDTJOF LUND-JOHANSEN and  
LEON W. TERSTAPPEN

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Appeal No. 1997-2319  
Application 08/147,707<sup>1</sup>

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ON BRIEF

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Before ROBINSON, SCHEINER and ADAMS, Administrative Patent Judges.

SCHEINER, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 1 through 3, 5 through 8, 10 and 11. Claims 4 and 9 are pending but have been withdrawn from consideration by the examiner.

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<sup>1</sup> Application for patent filed November 4, 1993.

Claims 1, 5, 6, 10 and 11 are illustrative of the subject matter on appeal and read as follows:

1. A method for identifying one or more populations of human progenitor cells, said populations comprising lymphoid, erythroid and myeloid progenitors, comprising the steps of labeling a sample of human cells containing said populations with a marker for CD34, a marker for CD38 and one or more markers for cell adhesion molecules and/or growth factor receptors and identifying said populations based upon the expression of each of the markers.

5. The method of claim 1 wherein said growth factor receptors are selected from the group consisting of SCFR, GM-CSFR, IL-6R, gp130/IL-6R and IL-7R.

6. A method for isolating one or more populations of human progenitor cells, said populations comprising lymphoid, erythroid and myeloid progenitors, comprising the steps of labeling a sample of human cells containing said populations with a marker for CD34, a marker for CD38 and one or more markers for cell adhesion molecules and/or growth factor receptors and isolating said populations based upon the expression of each of the markers.

10. The method of claim 6 wherein said growth factor receptors are selected from the group consisting of SCFR, GM-CSFR, IL-6R, gp130/IL-6R and IL-7R.

11. An isolated population of human progenitor cells prepared according to the method of claim 6.

The references relied on by the examiner are:

Terstappen et al. (Terstappen), "Sequential Generations of Hematopoietic Colonies Derived from Single Nonlineage-Committed CD34<sup>+</sup> CD38<sup>-</sup> Progenitor Cells," Blood, Vol. 77, pp. 1218-1227, 1991

Armitage et al. (Armitage), "Identification of a Novel Low-Affinity Receptor for Human Interleukin-7," Blood, Vol. 79, pp. 1738-1745, 1992

McClanahan et al. (McClanahan), "Hematopoietic Growth Factor Receptor Genes as Markers of Lineage Commitment during In Vitro Development of Hematopoietic Cells," Blood, Vol. 81, pp. 2903-2915, 1993

Claims 1 through 3, 5 through 8, 10 and 11 stand rejected under the first paragraph of 35 U.S.C. § 112, as based on a non-enabling disclosure. In addition, claims 1 through 3, 5 through 8, 10 and 11 stand rejected under 35 U.S.C. § 103 as unpatentable over Terstappen, McClanahan and Armitage. On consideration of the record, we reverse the rejection under 35 U.S.C. § 112, first paragraph, as well as the rejection under 35 U.S.C. § 103. However, we raise an additional issue for consideration upon return of the application to the examining group.

#### PROCEDURAL MATTERS

Initially, we note that appellants originally elected a particular species of the genus “cell adhesion molecules and/or growth factor receptors” in response to a requirement under 35 U.S.C. § 121 (paper no. 6). Thus, according to the examiner, “[t]he appealed claims have been examined with respect to the elected species, ‘IL-7R’.” Examiner’s Answer, page 2. That is, the claims have been examined as though each requires a marker for the IL-7 receptor. Accordingly, we review the examiner’s rejection and appellants’ response with this in mind.

#### DISCUSSION

##### Enablement

All of the claims on appeal stand rejected under 35 U.S.C. § 112, first paragraph as unenabled throughout their scope. The examiner’s concerns are three-fold.

The examiner acknowledges that the specification is enabling for “making” (which we take to mean identifying and/or isolating) cells positive for CD34, CD38 and

the high-affinity IL-7 receptor, but concludes that it is not enabling “for methods of making CD34<sup>-</sup>, CD38<sup>-</sup> and/or high-affinity-IL7R<sup>-</sup> cells.” Examiner’s Answer, page 3. We find this aspect of the rejection to be without merit, as the examiner has not explained why a cell which does not test positive for CD34, e.g., would or could not be identified as negative for that marker, and isolated on that basis.

In a similar vein, the examiner concludes that the specification is not enabling for “methods involving separation based upon expression of the low affinity IL-7 receptor.” According to the examiner, “two distinct IL-7 receptors are known in the art,” but “the disclosure makes reference to only one” and “does not particularly indicate which of the two IL-7Rs known in the art is the subject of teachings concerning ‘IL-7R’.” This is inconsistent with the examiner’s concurrent conclusion that the specification is enabling for “making” cells that are positive for the high-affinity IL-7 receptor. Examiner’s Answer, page 3. Moreover, the examiner has not explained why one skilled in the art would not be able to identify and/or isolate cells based on the low-affinity IL-7 receptor, since, as acknowledged by the examiner, both high and low affinity receptors were known in the art at the time of filing. Accordingly, we find this aspect of the rejection to be without merit as well.

Finally, the examiner concedes that the disclosure is enabling for using CD34<sup>+</sup>, CD38<sup>+</sup>, high-affinity-IL7R<sup>+</sup> cells since “such cells are lymphoid-committed” and one “would readily appreciate that a population of lymphocytes . . . would be useful, for example, to reconstitute lymphocyte populations in immunocompromised patients.”

Nevertheless, the examiner argues that “[t]he teachings provided in the disclosure do not teach the artisan how to use all the cell populations which can be selected by various combinations of the presence or absence of CD34, CD38, and all of the IL-7 receptors which were known in the art at the time of the invention” inasmuch as “cells corresponding to such subpopulations would have uncharacterized properties.”

Examiner’s Answer, page 4. While it is true that the specification does not discuss all of the cell populations which can be selected by various combinations of the presence or absence of CD34, CD38 and the IL-7 receptor, certainly a number of possibilities are characterized. For example, according to the specification (page 11), “the absence of expression of both IL-7R and IL-6R” on CD34<sup>+</sup>, CD38<sup>+</sup> cells “appears useful in identifying erythroid progenitors,” yet the examiner has not explained why one skilled in the art would not be able to use such cells to reconstitute erythroid populations.

It is well settled that the examiner bears the initial burden of providing reasons why a supporting disclosure does not enable a claim. In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971). We find that the examiner has not established a reasonable basis for questioning the enablement of the claims on appeal. Accordingly, the rejection of claims 1 through 3, 5 through 8, 10 and 11 under the first paragraph of 35 U.S.C. § 112 is reversed.

#### Obviousness

Claims 1 through 3, 5 through 8 and 10 are directed to a method for identifying or isolating one or more populations of human progenitor cells, “said populations

comprising lymphoid, erythroid and myeloid progenitors,” “based upon the expression” of CD34, CD38 and (as the result of an election of species) the IL-7 receptor. Claim 11 is directed to “[a]n isolated population of human progenitor cells” prepared according to the claimed method.

Hematopoietic stem cells are capable of both self-renewal and differentiation into a variety of hematopoietic lineages. Terstappen teaches that human bone marrow cells expressing the CD34 antigen are enriched for progenitor cells but represent a heterogeneous cell population containing both lineage-committed and nonlineage-committed cells (i.e., putative hematopoietic stem cells). Lineage-committed cells can be distinguished from nonlineage-committed cells by multiparameter flow cytometry (using fluorescently labeled monoclonal antibodies) based on differential expression of the CD34 and CD38 antigens. Essentially, CD34<sup>+</sup>, CD38<sup>+</sup> bone marrow cells are committed to either the erythroid, myeloid, or lymphoid cell lineage, while CD34<sup>+</sup> CD38<sup>-</sup> cells are nonlineage-committed. The various populations of CD34<sup>+</sup> CD38<sup>+</sup> lineage committed bone marrow cells are further distinguished by the appearance of the “lineage-associated antigens,” CD71, CD33 and CD10. That is, commitment to the erythroid lineage is marked by appearance of the CD71 antigen; commitment to the myeloid lineage is marked by the appearance of the CD33 antigen; and commitment to the B-lymphoid lineage is marked by the appearance of the CD10 antigen. Human thymus cells committed to the T-lymphoid lineage also express both CD34 and CD38,

as well as the T-lineage associated antigens CD5 and CD7. Terstappen, Abstract, Introduction and page 1225.

McClanahan describes PCR experiments assessing the levels of mRNA corresponding to various growth factor receptor subunits and protooncogenes in developing mouse hematopoietic cells. "Of the genes whose expression changed during in vitro differentiation, the IL-7R gene displayed the most dramatic increase at later states of development," thus, McClanahan suggests that "this may be evidence of lymphoid lineage commitment," although it is not known whether "all of the receptor mRNAs expressed in [embryonic stem] cells lead to the production of functional proteins, or if these molecules are expressed on the surface." Pages 2912-13.

Armitage describes monoclonal antibodies specific for IL-7 receptors.

According to the examiner (Examiner's Answer, pages 7 and 8, brackets in the original),

It would have been obvious to one of ordinary skill in the art . . . to perform three-color FACS protocols to isolate populations of human cells, employing CD34-, and CD38-specific mAbs, according to the method of Terstappen, and including as the third antibody one of the IL-7R-specific mAbs disclosed by Armitage in place of any of the third antibodies employed by Terstappen, because Terstappen teaches that CD34<sup>+</sup> CD38<sup>+</sup> cells are lineage committed, and because McClanahan teaches that the expression of mRNA for the [high affinity] IL-7R, which the artisan would reasonably have expected to correlate with the expression of the IL-7R protein on the surface of the cell, is likely to be characteristic of lymphoid commitment. The artisan accordingly would have expected that FACS selection for the expression of all three of these markers . . . would yield a population of lymphoid-committed hematopoietic progenitor cells.

We disagree. As set forth in In re Kotzab, 217 F.3d 1365, 1369-70, 55 USPQ2d 1313, 1316 (Fed. Cir. 2000):

A critical step in analyzing the patentability of claims pursuant to section 103(a) is casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field. [] Close adherence to this methodology is especially important in cases where the very ease with which the invention can be understood may prompt one “to fall victim to the insidious effect of a hindsight syndrome wherein that which only the invention taught is used against its teacher.” []

[T]o establish obviousness based on a combination of the elements disclosed in the prior art, there must be some motivation, suggestion or teaching of the desirability of making the specific combination that was made by the applicant. [citations omitted]

In other words, “there still must be evidence that ‘a skilled artisan, . . . with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed.’” Ecolchem Inc. v. Southern California Edison, 227 F.3d 1361, 1375, 56 USPQ2d 1065, 1075-76 (Fed. Cir. 2000).

Admittedly, this is a close case. McClanahan explicitly suggests that induction of IL-7R mRNA “may be evidence of lymphoid lineage commitment” in the mouse (page 2912), but we note that the suggestion is tempered somewhat by the acknowledgment that it is not known whether “all of the receptor mRNAs expressed in [embryonic stem] cells lead to the production of functional proteins, or if these molecules are expressed on the surface” (page 2913). Terstappen’s method, on the other hand, successfully and unambiguously identifies human CD34<sup>+</sup>, CD38<sup>+</sup> cells as lymphoid-committed using CD10 as a marker of lineage commitment. All things considered, we do not find

McClanahan's suggestion to be compelling enough to give one skilled in the art reason to replace Terstappen's reliable marker with one of less certain significance.

In our view, the references, at best, make it obvious to try to identify and/or isolate cells committed to the lymphoid-lineage by "including as the third antibody . . . IL-7R-specific mAbs . . . in place of any of the third antibodies employed by Terstappen," as proposed by the examiner. Nevertheless, it is well settled that "obvious to try" is not the standard under 35 U.S.C. § 103. See In re O'Farrell, 853 F.2d 894, 903, 7 USPQ2d 1673, 1680 (Fed. Cir. 1988). We find that the examiner's burden of establishing a prima facie case of obviousness has not been met. Accordingly, the rejection of the claims under 35 U.S.C. § 103 is reversed.<sup>2</sup>

#### OTHER ISSUES

We have reversed the examiner's rejection of claims 1 through 3, 5 through 8, 10 and 11 under 35 U.S.C. § 103, nevertheless, it is not clear from the record whether claim 11 was evaluated under the appropriate legal standards. Claim 11 is a product by process claim directed to "[a]n isolated population of human progenitor cells prepared according to the method of claim 6." It is well settled that "even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself." That is, "[t]he patentability of a product does not depend

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<sup>2</sup> We emphasize that our deliberations extend only to the elected species of the claimed invention; we take no position on the relevance of the cited references to any other embodiment of the invention.

on its method of production,” and “[i]f the product . . . is the same as . . . a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.” In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted).

Claim 11 encompasses a number of cell populations selected by various combinations of the presence or absence of CD34, CD38 and the IL-7 receptor. While the examiner states that “[t]he invention involves the selection of cell subpopulations which were not previously available to the art” (Examiner’s Answer, sentence bridging pages 4 and 5), it is not clear to us that, say, a population of lymphoid-committed cells isolated “based upon the expression” of CD34, CD38 and the IL-7 receptor, would be any different than an isolated population of lymphoid-committed cells isolated on the basis of CD34, CD38 and CD10 expression. Upon return of the application to the examining group, we recommend that the examiner, if he has not already done so, evaluate the patentability of claim 11 in light of the correct legal standards and the foregoing remarks.

#### CONCLUSION

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In conclusion, for the reasons set forth in the body of this opinion, the rejections of the claims under 35 U.S.C. § 112, first paragraph and § 103 are reversed. Additionally, we raise an issue for consideration on return of this application to the examining group.

REVERSED

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Douglas W. Robinson	)	
Administrative Patent Judge	)	
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	)	BOARD OF PATENT
Toni R. Scheiner	)	
Administrative Patent Judge	)	APPEALS AND
	)	
	)	INTERFERENCES
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